Human Embryonic Stem Cell Differentiation to Trophoblast: Basic Biology and Clinical Translation to Improve Human Fertility

Grant Award Details

Human Embryonic Stem Cell Differentiation to Trophoblast: Basic Biology and Clinical Translation to Improve Human Fertility

Grant Type: SEED Grant

Grant Number: RS1-00207

Investigator:

Name:	Linda Giudice
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Fertility

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $614,784

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Human Embryonic Stem Cell Differentiation to Trophoblast: Basic Biology and Clinical Translation to Improve Human Fertility

Public Abstract:

In addition to the important potential applications for transplantation and treatment of chronic diseases, human embryonic stem cells (hESC) are also a valuable resource to study early human development relevant to fertility and healthy pregnancies. After fertilization, the human zygote undergoes cell divisions and ultimately becomes the blastocyst that has an inner cell mass and a trophectoderm shell, the precursor of the placenta and the tissue that attaches to the surface of the lining of the uterus, initiating the process of embryonic implantation. After attachment, the placental cells invade into the mother's uterine lining to secure the pregnancy and to establish the placenta for fetal growth and development. Abnormalities in the implantation process can lead to infertility, small babies, and pre-eclampsia that have significant health consequences for women and children. It has been extremely difficult to study the early phases of human implantation because of lack of available tissues (human blastocysts), restrictions on using federal funds for experimentation on human embryos, and the advanced differentiated state (i.e., beyond the trophectoderm stage) of placental cells derived from early terminations of pregnancies. This grant focuses on differentiating hESC to trophectoderm, development of this specialized tissue, and interactions of it with the maternal uterus, as a model of events in the early stages of human implantation.

hESC and human embryos are essential to this project. We propose to study biological processes, biochemical pathways, and key genes expressed during the transition of hESC to trophectoderm and compare them with those of the outer shell isolated from human blastocysts. We shall also identify secreted products from these specialized cells and investigate their effects on human endometrial epithelial cells to get information about how the blastocyst communicates with the maternal uterine lining just as it is about to implant. Finally, we shall identify secreted biomarkers that can be used in future studies as a diagnostic to assess embryo quality in human IVF and as therapies to enhance endometrial receptivity to embryonic implantation in women with implantation-based infertility. This proposal has promise for important translation to improve practical issues in human infertility and pregnancy disorders associated with abnormal embryonic implantation.

Statement of Benefit to California:

We believe that our proposal has the potential to be of benefit to California and its citizens from three perspectives: 1. Basic knowledge to impart to our students. This proposal has the potential to elucidate genes, their products, biochemical pathways, and biological processes involved in the earliest stages of implantation – specifically in the shell of the blastocyst and its communication with the maternal uterine endometrium. This could add significantly to the education of our students in this important field of human development. 2. Clinical benefits from development of a diagnostic for the implantation potential of an embryo for individuals undergoing in vitro fertilization/embryo transfer, and also to improve the ability of the maternal uterus to accept and nourish an implanting embryo, important in women who have implantation-based infertility and/or a history of implantation-based pregnancy disorders, such as pre-eclampsia, intrauterine fetal growth restriction, and miscarriage.3. Commercial benefit. The development of a diagnostic test of the implantation potential of an embryo in clinical practice and of developing therapies to enhance implantation can be of major benefit to the economy of our State.
